

IT IS CLAIMED:

1. A method of administering to a selected region of a patient's respiratory tract, an amount of human gamma-interferon (γ -IFN) having a known, selected gamma-interferon biological activity and molecular size distribution, said method comprising,

placing an aqueous γ -IFN solution having a known, selected γ -IFN biological activity, and containing a stabilizing agent and a dispersing agent, against a plate having defined-size openings,

forcing the solution through said openings under conditions effective to form aqueous droplets having (a) a volume mean diameter in a selected size range selected from the group consisting of (i) less than 1 microns, (ii) 1-3 microns, (iii) 3-5 microns, (iv) 5-10 microns, (v) greater than 10 microns, and (vi) two or more of the size ranges, (b) a γ -IFN biological activity substantially the same as that of the solution, and (c) a γ -IFN molecular size distribution substantially the same as that of the solution; and

delivering the aqueous droplets to a patient's respiratory tract.

2. The method of claim 1, wherein the biological activity of the γ -IFN in solution and droplet form is determined by (i) the ability of γ -IFN to stimulate CD64 antigen expression in cultured enriched human monocytes, or (ii) the biological activity of the γ -IFN in solution and droplet form is determined by the ability of γ -IFN to stimulate HLA-DR antigen expression in cultured human monocytes.

3. The method of claim 2, wherein said solution contain at least 1 million International units of gamma-IFN per ml.

4. The method of claim 1, wherein said solution includes mannitol as a stabilizing agent.

5. The method of claim 4, wherein said mannitol is present in an amount between 5-15 mM.

6. The method of claim 1, wherein said solution includes polysorbate as a
5 dispersing agent.

7. The method of claim 6, wherein the polysorbate is present in an amount between 50 and 200 mg/liter.

10 8. The method of claim 1, wherein the plate against which the solution is placed is vibrating at an amplitude and frequency effective to form droplets of the defined, selected size.

9. The method of claim 1, wherein the plate against which the solution is
15 placed is stationary, the solution is placed against the plate under pressure, thus forming streams of extruded solution, and said streams are broken into desired, selected-size particles by passing a stream of gas over the plate.

20 10. The method of claim 1, for use in treating interstitial lung diseases, infectious diseases of the lung, bronchial constrictive diseases, and cystic fibrosis, wherein said forming is effective to produce droplets in the 1-3 micron size range.

25 11. The method of claim 10, wherein said forming is also effective to produce particles in the 3-5 micron size range.

12. The method of claim 10, for use in treating cystic fibrosis, wherein said forming is effective to produce particles in the size range less than 1 micron.

30 13. The method of claim 1, for use in treating disease conditions that are responsive to systemically administered γ -IFN, wherein said forming is effective to produce droplets in the 1-3 micron size range.

14. The method of claim 13, wherein said forming is also effective to produce particles in the 3-5 micron size range.

5 15. A liquid-droplet aerosol composition for delivery to a patient's respiratory tract

(a) formed by placing an aqueous γ -IFN solution having a known, selected γ -IFN biological activity, and containing a stabilizing agent and a dispersing agent, against a plate having defined-size openings, and forcing the solution through said openings under conditions effective to form aqueous droplets having (a) a volume mean diameter in a selected size range selected from the group consisting of (i) less than 1 microns, (ii) 1-3 microns, (iii) 3-5 microns, (iv) 5-10 microns, (v) greater than 10 microns, and (vi) two or more of the size ranges, (b) a γ -IFN biological activity substantially the same as that of the solution, and (c) a γ -IFN molecular size distribution substantially the same as that of the solution; and

(b) characterized by an aerosol of aqueous droplets having (a) a volume mean diameter in a selected size range selected from the group consisting of (i) less than 1 microns, (ii) 1-3 microns, (iii) 3-5 microns, (iv) 5-10 microns, (v) greater than 10 microns, and (vi) two or more of the size ranges, (b) a γ -IFN biological activity substantially the same as that of the solution, and (c) a γ -IFN molecular size distribution substantially the same as that of the solution.

16. The composition of claim 15, wherein said solution contain at least one million International units of gamma-IFN/ml, as measured by (i) the ability of γ -IFN to stimulate CD64 antigen expression in cultured enriched human monocytes, or (ii) the biological activity of the γ -IFN in solution and droplet form is determined by the ability of γ -IFN to stimulate HLA-DR antigen expression in cultured human monocytes.

17. The composition of claim 15, wherein said solution includes mannitol as a stabilizing agent.

18. The composition of claim 17, wherein said mannitol is present in an amount between 5-15 mM.

19. The composition of claim 15, wherein said solution includes
5 polysorbate as a dispersing agent.

20. The composition of claim 19, wherein the polysorbate is present in an amount between between 50-200 mg/liter weight percent.

10 21. The composition of claim 15, wherein the solution has a viscosity at room temperature of less than 2Cp.